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THE USE OF HYPOXIC AND CARBON DIOXIDE SENSITIVITY TESTS TO PREDICT THE INCIDENCE AND SEVERITY OF ACUTE MOUNTAIN SICKNESS IN SOLDIERS EXPOSED TO AN ELEVATION OF 3800 METERS

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UNITED STATES ARMY
MEDICAL RESEARCH & DEVELOPMENT COMMAND

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THE USE OF HYPOXIC AND CARBON DIOXIDE SENSITIVITY TESTS TO PREDICT THE INCIDENCE AND SEVERITY OF ACUTE MOUNTAIN SICKNESS IN SOLDIERS EXPOSED TO AN ELEVATION OF 3800 METERS.

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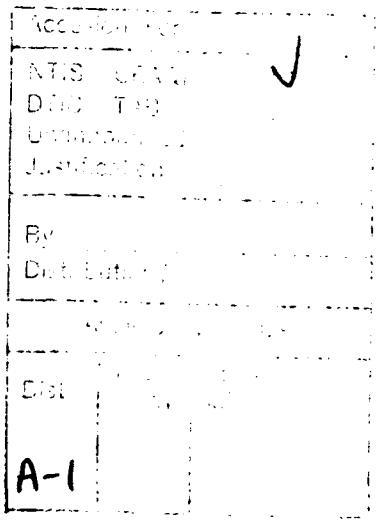

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February 1991

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Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

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13 ABSTRACT (Maximum 200 words)

Acute mountain sickness (AMS) is characterized by headache, nausea, and dizziness with individual differences occurring susceptibility. At any altitude, there will be individuals who will show little or no symptoms while others will be severely incapacitated. Previous studies have shown that individuals with no symptoms of AMS tend to ventilate more than those who develop severe symptoms. The main objective of this study was to determine if susceptibility to AMS can be predicted from ventilatory responses to breathing hypoxic and carbon dioxide gas mixtures for 7-10 minutes prior to an altitude exposure. Another objective was to determine if there was a difference between cigarette smokers and nonsmokers in susceptibility. Forty-seven soldiers (25 smokers and 22 nonsmokers) performed an isocapnic hypoxic ventilatory response (HVR) test and a hypercapnic ventilatory response (HCVR) test at Ft. Riley, KS (450 m) prior to being deployed to the Santa Lucia Base Camp, Potosi, Bolivia (3500 to 4050 m). AMS symptoms were assessed in Bolivia by the self-administered Environmental Symptoms Questionnaire during the first two days of exposure. Eighteen of 47 soldiers (38%) developed AMS. There was no relationship between either of the ventilatory tests and the subsequent development of AMS regardless of smoking history. The results suggest that the use of the HVR and HCVR tests to preselect individuals who will develop AMS at moderate altitudes is not warranted. It was also found that there was no difference in the incidence rate (40% vs 36%) or severity of AMS between smokers and nonsmokers.

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FOREWORD

A Task Force (Fuertes Caminos, FC-90) of approximately 450 U.S. soldiers and marines were exposed to altitudes ranging from 3500 to 4050 m for nearly five months on the Andean altiplano, in the vicinity of Potosi, Bolivia, South America to participate in a large construction project. The Task Force consisted principally of engineers and road builders assembled from Ft. Riley, KS and represented the largest commitment of U.S. troops ever exposed to such high altitudes during peacetime or war. The troops conducted an operational scenario comparable to one usually conducted under sea-level conditions.

Therefore, a unique opportunity existed to study the incidence and severity of altitude-related illnesses, decrements in physical and mental performance, and changes in dietary habits. The 450 army and marine participants of FC-90 were medically cleared by physicians prior to inclusion in the construction project. Of these, a subsample of approximately 100 males were preselected by the Task Force commander to participate in studies conducted by the Altitude Physiology and Medicine Division and the Military Nutrition Division of the U.S. Army Research Institute of Environmental Medicine, Natick, MA. All gave their voluntary, informed consent to participate in the studies.

Some studies were conducted only prior to or only after deployment to Bolivia, while other studies were conducted at both times. Presented in this report will be the results of hypoxic and carbon dioxide sensitivity tests performed at Ft. Riley and the acute mountain sickness assessments conducted in Bolivia. The results of the other studies will be forthcoming.

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The authors wish to thank David A. Burgoon for his technical expertise and limitless patience in modifying a sophisticated software package for the unique requirements of the ventilatory collection system used in this study.

SUMMARY

Acute mountain sickness (AMS) is characterized by headache, nausea, and dizziness. Individual differences occur in AMS susceptibility. At any altitude, there will be individuals who will show little or no symptoms while others will be severely incapacitated. Previous studies have shown that individuals with no symptoms of AMS tend to ventilate more than those who develop severe symptoms. The main objective of this study was to determine if susceptibility to AMS can be predicted from ventilatory responses to breathing hypoxic and carbon dioxide gas mixtures for 7 to 10 minutes prior to an altitude exposure. Another objective was to determine if there was a difference between cigarette smokers and nonsmokers in susceptibility. Forty-seven soldiers (25 smokers and 22 nonsmokers) performed an isocapnic hypoxic ventilatory response (HVR) test and a hypercapnic ventilatory response (HCVR) test at Ft. Riley, KS (450 m) prior to being deployed to the Santa Lucia Basecamp, Potosi, Bolivia, South America (3500 to 4050 m). AMS symptoms were assessed in Bolivia by the self-administered Environmental Symptoms Questionnaire during the first two days of exposure. Eighteen of 47 soldiers (38%) developed AMS. There was no relationship between either of the ventilatory tests and the subsequent development of AMS regardless of whether the soldiers were smokers or nonsmokers. The results suggest that the use of the HVR and HCVR tests to preselect individuals who will develop AMS at moderate altitudes is not warranted. It was also found that there was no difference in the incidence rate (40% vs 36%) or severity of AMS between smokers and nonsmokers.

INTRODUCTION

Acute mountain sickness (AMS) is a symptom complex which includes headache, nausea, dizziness, weakness, and insomnia (Johnson and Rock 1988; Malconian and Rock 1988). In general, the symptoms usually become noticeable after 4 to 8 hours of exposure, reach their peak severity within the first 24-48 hours and then gradually recede over the ensuing 2-4 days (Malconian and Rock 1988). The symptoms become more pronounced as the rate of ascent and the final elevation are increased (Johnson and Rock 1988).

The deleterious impact of altitude-induced morbidity, especially AMS, represents a significant potential loss of unit strength and can seriously jeopardize the successful attainment of a unit's mission or objectives. Official reports have shown that fifty to eighty percent of troops rapidly brought to altitudes in excess of 4000 m will be afflicted with AMS (Dept. of the Army 1975). Many of these individuals were totally incapacitated for days. Despite the fact that AMS is a common disorder, its etiology remains unclear (Johnson and Rock 1988).

Presently, US Army doctrine for prevention of AMS is a combination of staging (slow ascent to final elevation with frequent sojourns at lower elevations), and administration of acetazolamide (Dept. of the Army 1975; Robinson et al. 1974). When the two are used in combination, an 85% reduction in symptoms occurs (Evans et al. 1976). However, in many military operations staging may not be feasible. Acetazolamide, without staging reduces symptomatology by only 20-25% (Evans et al. 1976; Hackett 1980). Other medications such as dexamethasone and spironolactone have recently shown promise as possible prophylactic agents (Johnson et al. 1984; Larsen et al. 1986), but because of potential side effects or lack of clinical trials, they are not in widespread use. Therefore, alternative methods and procedures to help lessen the incidence and severity of AMS must be employed.

Individuals seem to have different sensitivities to AMS (Hackett et al. 1976; Johnson and Rock 1988). At any given altitude, there will be some individuals who will show little or no symptoms of AMS while others will be severely incapacitated (Malconian and Rock 1988). Therefore, another strategy which could be employed to help reduce the incidence of AMS would be to deploy to high mountainous regions only those individuals known to be resistant to AMS. To date, no known method or procedure exists which would allow such a preselection.

In several studies, however, an inverse association between the magnitude of the increase in ventilation at altitude and the symptoms of AMS has been observed, i.e., those who have a large increase in ventilation tend to demonstrate less severe symptoms of AMS (Anholm et al. 1979; Hackett et al. 1977; King and Robinson 1972). Moreover, it has been reported that there is a direct relationship between the magnitude of increase in ventilation during the first few days at altitude (Huang et al. 1984; King and Robinson 1972; Moore et al. 1984) and ventilatory responsiveness to acute ventilatory challenges at sea level (both hypoxia and carbon dioxide). When the results of these studies are considered collectively, it is clear that there seems to be interrelationships between ventilation at altitude, AMS, and the ventilatory responses to acute hypoxic and carbon dioxide (CO_2) challenges at sea level. Therefore, it may be possible to screen for individuals highly susceptible to AMS prior to the exposure to high altitude by evaluating their responses to hypoxic and/or CO_2 chemosensitivity tests at sea level.

Results from several studies which utilized individuals exposed to terrestrial or simulated altitudes in excess of 4300 m seem encouraging (Huang et al. 1984; King and Robinson 1972; Moore et al. 1984; 1986). However, studies that have directly related pre-altitude ventilatory sensitivities to AMS utilized small numbers of subjects whose data were either selected for analyses after their illness had occurred (King and Robinson 1972) or whose subjects were selected based on prior knowledge that they would or would not get sick (Moore et al. 1986). It has not been determined if it is possible to preselect a subgroup of individuals who are likely to get sick at moderate altitudes from a larger group of individuals whose susceptibility to AMS is unknown using the results of ventilatory sensitivity tests conducted at low altitudes prior to deployment.

The primary objective of this investigation was to determine if individual susceptibilities to AMS can be predicted from ventilatory responses to hypoxic and CO_2 sensitivity tests performed prior to an altitude exposure. A secondary objective was to determine if there are differences in AMS susceptibility between individuals who smoke and don't smoke cigarettes.

METHODS

Study Design

This study was divided into two phases of testing: A pre-altitude phase conducted over a two-week period in April 1990 at Fort Riley, Kansas (P_B = 720 torr), and an altitude phase which was conducted in July-August 1990 for the first two days of residence at the Santa Lucia basecamp in Bolivia. The barometric pressures ranged from 502-508 torr (3500-3800 m) at the basecamp to 479 torr (4050 m) at the construction site.

Testing Procedures

Subjects were not allowed to eat, drink, or smoke at least three hours prior to the ventilatory tests. The isocapnic hypoxic ventilatory response (HVR) and the hypercapnic ventilatory response (HCVR) tests were performed with the reclining subject breathing through a low resistance respiratory valve. Ambient temperature was maintained at 23.0 °C (range: 21.5 to 24.5 °C) during the HVR and HCVR tests. End-tidal partial pressures of oxygen ($PetO_2$) and carbon dioxide ($PetCO_2$) were monitored continuously from the mouthpiece using a S-3A (Applied Electrochemistry Inc) and a LB-2 (Beckman Instruments Inc), respectively. Expired air was directed either through a Pneumoscan spirometer (K and E Engineering) for measurement of minute ventilation ($\dot{V}E$) prior to the HVR and HCVR tests or into a wedge spirometer (Medical Science) for calculation of breath-by-breath $\dot{V}E$ during the HVR and HCVR tests. Oxygen saturation (SaO_2) was monitored using ear oximetry (Hewlett-Packard Co.). Output voltages from the S-3A, LB-2, wedge spirometer, and ear oximeter were simultaneously collected, displayed on a computer screen, and stored into a Lotus file (Lotus 1-2-3, Lotus Development Corp) at the rate of 20 times/sec during the HVR and HCVR tests.

After a two to three minute resting $\dot{V}E$ was collected and a $PetCO_2$ was determined, the subject was switched into the closed spirometry system for determination of HVR (Figure 1). The $PetCO_2$ of the subject was maintained by adjusting a variable bypass valve to regulate the flow of expired gas either through or bypassing a CO_2 absorber (barium hydroxide lime, Baralyme, Chemetron Medical Products). The subject's rate of oxygen uptake slowly reduced the $PetO_2$ from about 105 torr (SaO_2: 92-96%) to just below 40 torr. The test was terminated when the subject's SaO_2 fell below 70% (usually in seven to ten minutes). At the conclusion of the collection period, the curve showing the relationship of the increase in ventilation to the reduction in saturation was displayed. The HVR was

calculated (using linear regression) as the absolute value of the slope of the relationship.

Preparation for the HCVR test was begun at the completion of the HVR test. The system was flushed with ambient room air. Then the "bag in the box" was totally evacuated and refilled with 100% O_2. After the mouthpiece and noseclip were placed and the subject was quietly breathing ambient air, he was switched into the closed system whose total gas concentration was a combination of the volume of the 100% O_2 in the "bag in the box" and the volumes of the dead spaces within the mouthpiece, valves, and hoses. In three to five breaths, $PetO_2$ increased from about 105 torr to 269-337 torr and remained at this level for the duration of the HCVR test. Because the CO_2 absorber was voluntarily bypassed, the $PetCO_2$ slowly increased from about 45 torr to the target value (>60 torr). The duration of the test was about five to ten minutes. At the conclusion of the HCVR test, the curve relating the increase in ventilation to the increase in $PetCO_2$ was displayed. Using linear regression, the value for HCVR was determined as the slope of the relationship.

The Environmental Symptoms Questionnaire (ESQ) was used to assess AMS symptomatology (Sampson et al. 1980). The ESQ is a 67-item inventory designed to quantitate symptoms induced by altitude and other stressful environments and conditions (Sampson et al. 1983). The ESQ was self-administered utilizing a pencil and paper presentation on four occasions. The first time was prior to any testing in Kansas. The remaining three times were in South America. The first ESQ was administered in Bolivia while the subjects were on a train en route from Lapaz (4050 m) to Potosi (3500 m) after having been at altitude for nine hours. The second and third ESQs were administered at basecamp after the subjects had been at altitude for 33 hours and 45 hours, respectively. The subjects acknowledged each of the items with responses coded in the range from 0 ("not at all") to 5 ("extreme"). At the completion of each questionnaire, the numerical values for the responses were tabulated and two statistically-weighted factor groups: AMS-c ("cerebral") and AMS-r ("respiratory") were calculated. These groups were previously derived using image factoring and oblique rotation on 650 ESQs completed at altitude (Sampson et al. 1983). AMS-c and AMS-r are defined by eleven and twelve items, respectively. For example, the leading symptoms under AMS-c include "feeling sick", "feeling hungover", and "headache", while symptoms such as "hard to breathe", "short of breath", and "hurts to breathe" help define AMS-r. Both factor scores have been shown to be valid indicators of altitude sickness when the weighted values AMS-c and AMS-r exceed 0.7 and 0.6, respectively (Sampson et al. 1983). For purposes of this study, a subject was considered to have developed AMS if either one or both of the two factor scores as calculated from any of the three ESQs administered in Bolivia exceeded their

respective criterion values for altitude sickness.

For this study a total of 67 subjects completed an ESQ, and the HVR and HCVR tests in Kansas. Thirty-one were nonsmokers (never smoked cigarettes) and 36 were smokers (currently smoking at least 10 cigarettes/day). It was anticipated that the entire group would be deployed to Bolivia so that their symptomatology could be assessed. However, ESQs were administered to only 54 individuals from the original group of 67. Of these, 24 were nonsmokers and 30 were smokers. Most of the missing individuals were never deployed and a few could not be located in basecamp in time to have any of the ESQs administered. Also, seven individuals voluntarily took acetozolamide (Diamox) prior to and during deployment to Bolivia. Because acetazolamide affects ventilation and reduces the severity of AMS symptoms (Evans et al. 1976; Malconian and Rock 1988), it was decided to eliminate these individuals from the analyses. Thus, our final sample for analyses included a total of 47 individuals (22 nonsmokers and 25 smokers).

Linear regression was utilized to determine the relationships between the factor scores and the ventilatory tests. Independent t-tests were used to determine if differences in physical characteristics and ventilatory variables existed between nonsmokers and smokers. Statistical significance for all analyses was established at $p<0.05$.

RESULTS

The physical characteristics of the test subjects are presented in Table 1 as an entire group ("All", n=47) and as subgroups classified as nonsmokers and smokers. There were no statistically significant differences between smokers and nonsmokers in age, height, and body weight ($p>0.10$). In Table 2 are the values for $\dot{V}E$, $PetCO_2$, HVR, and HCVR obtained in Kansas. The only significant difference between nonsmokers and smokers was a lower $\dot{V}E$ for the smoking group.

The correlation coefficient for the relationship between HVR and HCVR was $r = 0.59$ ($p<0.01$) for the entire group. The relationships between HVR and HCVR were not meaningfully altered when the values obtained from the nonsmokers ($r = 0.63$, $p<0.01$) and smokers ($r = 0.59$, $p<0.01$) were analyzed separately.

The factor scores, AMS-c, and AMS-r, calculated from the ESQ were significantly greater in Bolivia relative to the values obtained in Kansas ($p<0.05$). Table 3 presents the

results from the ESQ for AMS-c and AMS-r obtained in Bolivia. There were no significant differences between nonsmokers and smokers in the two scores. Moreover, the mean values for AMS-c and AMS-r did not exceed the criterion scores of 0.7 and 0.6, respectively for AMS either for the entire group or for the two subgroups. The range of values for AMS-c and AMS-r for the nonsmokers and smokers were similar.

Table 4 presents the percentages of those who did and did not exceed the criterion scores for AMS-c and/or AMS-r. Both nonsmoker and smoker subgroups had a similar percentage of subjects exceeding the criterion score for AMS-c (36% vs 32%) whereas smokers had more than twice the percentage of nonsmokers exceeding the criterion score for AMS-r (40% vs 18%). Nevertheless, the percentage of subjects in each subgroup considered to have developed AMS was similar (36% vs 40%) based on the criterion value being exceeded for at least one of the two factors. In all, 18 of the 47 subjects (38%) tested were considered to have developed AMS.

There were no statistically significant differences determined in the mean values for $\dot{V}E$, $PetCO_2$, HVR, or HCVR between those who developed AMS (n=18) and those who did not (n=29). There were also no significant differences in the mean values found between those who developed AMS and those who didn't when the subjects were divided into nonsmoking and smoking subgroups (Table 5). The range of values for HVR and HCVR in those who did and did not develop AMS were not consistent between the smokers and the nonsmokers. For example, the range of values for HVR in the nonsmoking group who did NOT develop AMS was approximately equal to the range of those in the smoking group who DID develop AMS. The range of values for HCVR was more similar between the four subgroupings.

Our primary purpose in conducting this study was to determine if the results from ventilatory sensitivity tests performed at a low altitude could be used to predict who would get sick during the first two days of exposure to a moderate altitude. From the results presented in Table 6, it is apparent that it is not possible under the conditions of the present study. All of the relationships were poor ($r<0.18$, $p>0.30$) between the ventilatory variables and either one or both of the factor scores. The relationships did not improve when the subjects were subdivided into nonsmoking and smoking groups.

DISCUSSION

The results from previous studies had suggested that a diminished hypoxic and/or an increased CO_2 responsiveness as measured during ventilatory sensitivity tests conducted at a low altitude could provide a means to determine *a priori* who would develop AMS on subsequent exposure to a higher altitude (Anholm et al. 1979; King and Robinson 1972; Moore et al. 1984; 1986). However, we were unable to find a relationship between HVRs and/or HCVRs, and the development of AMS. The lack of a relationship was also maintained when nonsmokers and smokers were analyzed independently. Moreover, we were unable to discern differences in ventilatory sensitivity values after the subjects were dichotomized into sick and well groups.

In two previous studies (King and Robinson 1972; Moore et al. 1986), it was determined that individual differences in ventilatory sensitivities were related to differences in ventilation and AMS symptomatology during subsequent hypobaric exposures. The conclusions derived from these "successful" studies clearly disagree with our results. However, there are several important differences between these previous studies and the current study to suggest that the results may not be mutually exclusive. In both studies (King and Robinson 1972; Moore et al. 1986) the test subjects were preselected to be representative of a "sick" group and a "well" group. In one study which was conducted at 4300 m, only the ventilatory results of the five sickest and the five most well were compared even though the study was conducted on a total of twenty four individuals (King and Robinson 1972). Any data of the remaining 14 subjects were not reported and it was not mentioned if an attempt was made to determine if a relationship existed between the results of the HVR test and subsequent sickness. In the other study, conducted at 4800 m, hypoxic and CO_2 sensitivity tests were performed on individuals known from previous medical histories to be either symptomatic or asymptomatic to AMS (Moore et al. 1986). In the present investigation, all of the subjects tested were included in the analyses. There was no attempt to determine "the sickest of the sick" and compare their results to those who did not get sick. We felt that our approach was less biased and more realistic in an effort to determine if it is possible to predict the likelihood of developing AMS.

Thirty-eight percent of the 47 subjects tested in the present study were considered to have developed AMS, an overall proportion agreeing with the values reported in the literature for similar elevations (Evans et al. 1976; Hackett et al. 1976; Johnson and Rock 1988; Robinson et al. 1974). However, it was somewhat surprising to determine that there was little difference in the incidence of AMS between smokers and nonsmokers. Theoretically, smokers should have a higher risk of suffering more severe symptoms of

AMS at high altitude because increased levels of carboxyhemoglobin typically found in smokers could interfere with the combining of oxygen with hemoglobin and compromise oxygen transport (West 1985). While the incidence of smokers who developed AMS as defined by AMS-r was greater than nonsmokers (40% vs 18%), the overall incidence rate of AMS as defined by exceeding either the criterion values for AMS-c and/or AMS-r did not differ between groups (36% vs 40%). These results seem to suggest that smokers have more respiratory problems within the first two days at altitude, but not necessarily a higher incident rate of AMS.

The severity of illness was relatively mild in those who were considered to be sick. Even the individual who was determined to be the sickest had scores for AMS c and AMS-r of 1.63 and 1.50, respectively. The severity of illness as reflected by these values is only considered to be between "slight" and "somewhat" on the verbal rating scale of the ESQ. In previous studies relating ventilatory sensitivity to AMS (King and Robinson 1972; Moore et al. 1986), AMS symptomatology was much worse as reflected by the numbers of individuals who had to depart early from the experiment due to severe illness; all five in one study (King and Robinson 1972), and five of eight in the other (Moore et al. 1986). However, the altitudes were 4300 m or higher and the severity of the AMS symptomatology would be expected to be greater (Johnson and Rock 1988). In the present study, because the severity of illness was mild, the range of values reflecting illness (the scores for AMS-c and AMS-r) was not as large as the range of the results of the HVR and HCVR tests by a factor of approximately two to three (Tables 2,3,5). Differences in variation between two variables reduces the ability to relate one variable to the other (Sokal and Rohlf 1987). Therefore, a major reason for the inability to predict individual susceptibility to AMS from the results of ventilatory sensitivity tests could be due to the lack of spread in the range of sickness scores secondary to the mild degree of hypoxic stress at this moderate altitude. If this line of reasoning is correct, and if it is considered in the context of the previous "successful" studies, then it would suggest that the use of HVR and HCVR tests for the purpose of differentiating AMS susceptibility be restricted to altitudes in excess of 4300 m.

CONCLUSIONS

The mean values and the range of values for the HVR and HCVR tests were similar in smokers and nonsmokers prior to deployment. The incidence rate for the development of AMS at altitude (3800 m) between smokers and nonsmokers was also similar (40% and 36%). However, the difference in severity of AMS was small between the least and most affected in each group. In fact, the range of values for AMS symptomatology was narrower than the range of values for the ventilatory sensitivity tests by a factor of approximately two to three. Heterogeneity of variances between the symptom scores and the ventilatory sensitivity scores may have been the primary reason for the inability to predict individual susceptibility to AMS. These results suggest that the use of HVR and HCVR tests to discriminate between those individuals likely and unlikely to develop AMS be restricted to trials where the altitudes will be in excess of 4300 m.

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Figure 1

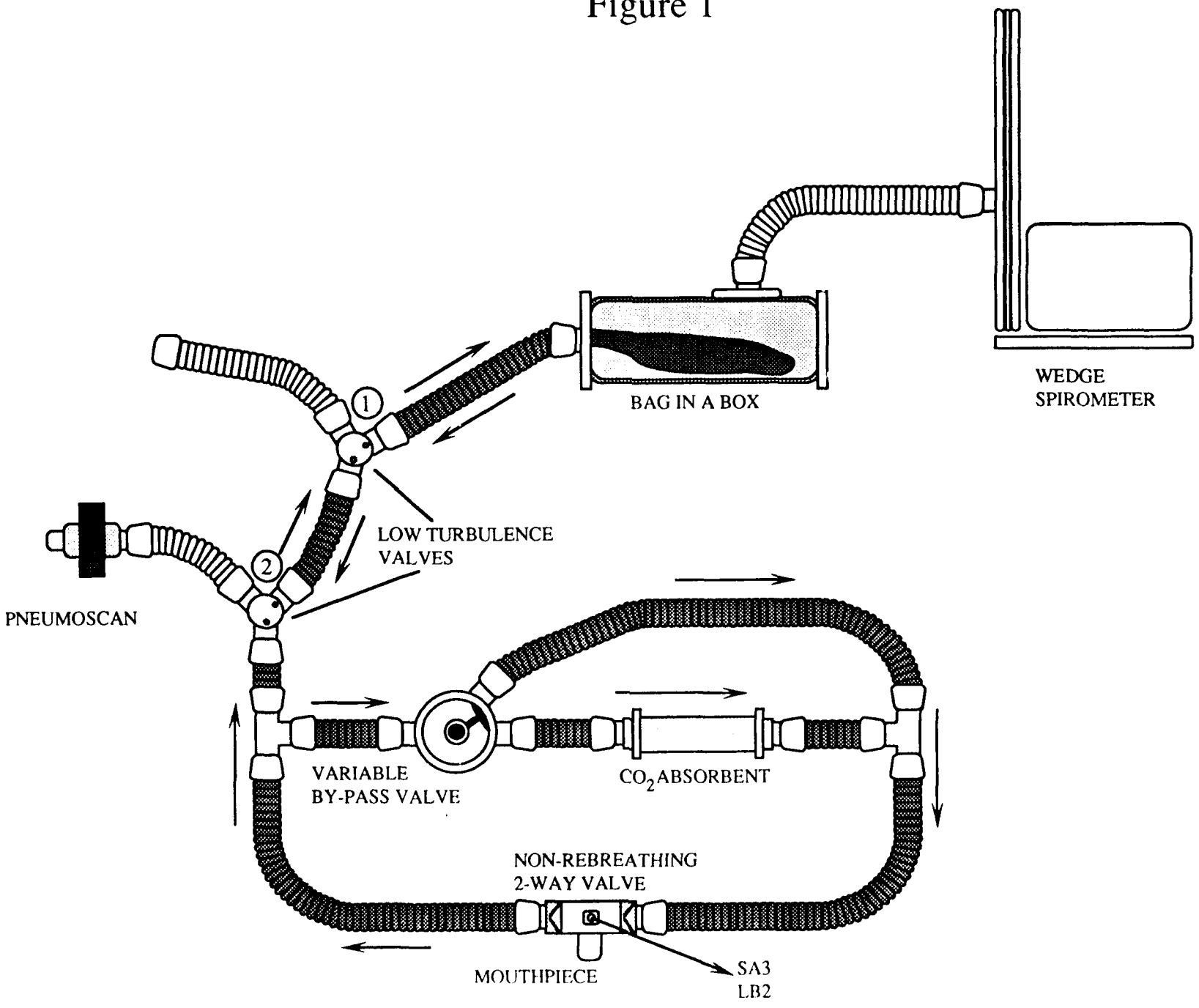
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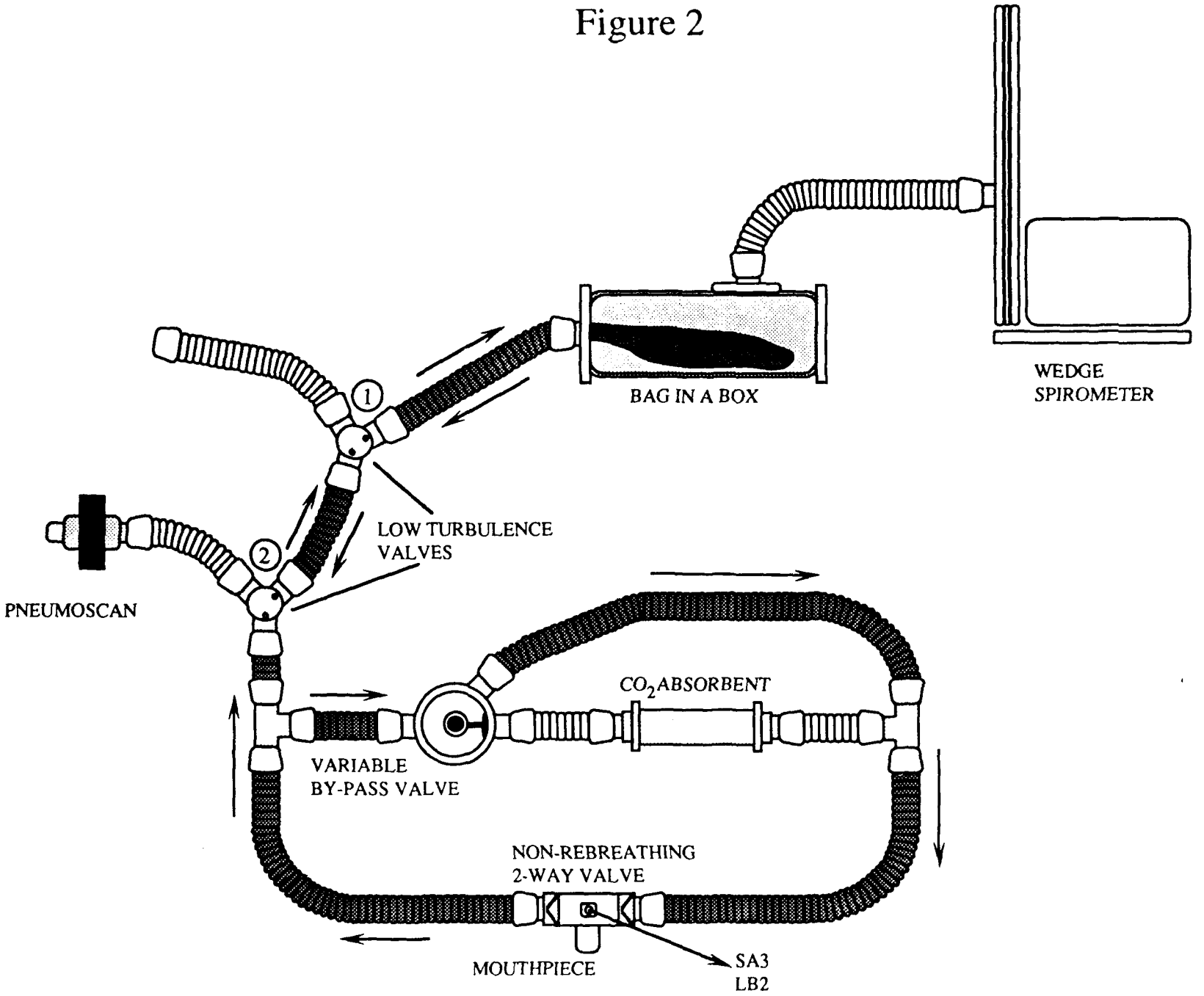
Figure 2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SA3
LB2

FIGURE LEGENDS

Figure 1: Flow diagram of the closed system for the determination of isocapnic hypoxic ventilatory response (HVR). Expired air was directed from the mouthpiece, through valves #1 and #2, and into the "bag in the box". Inspired air was rebreathed from the "bag in the box", through the two low turbulence valves, through a manually-controlled variable by-pass valve at the beginning of a two-tier parallel circuit. To decrease $PetCO_2$, inspired air was directed through the CO_2 absorber; to increase $PetCO_2$, expired air was directed though the other path.

Figure 2: Flow diagram of the closed system for the determination of hypercapnic ventilatory response (HCVR). Ventilation was directed from the mouthpiece, through valves #1 and #2, and into the "bag in the box". Inspired air was rebreathed from the "bag in the box", through the low turbulence and variable by-pass valves, and around the CO_2 absorbent to allow the CO_2 concentration to slowly increase.

Table 1

PHYSICAL CHARACTERISTICS OF THE TEST SUBJECTS

	ALL (n=47)	NONSMOKERS (n=22)	SMOKERS (n=25)
AGE (yr)	25.2 ± 5.8	25.2 ± 6.8	25.2 ± 4.7
HEIGHT (cm)	176.3 ± 7.4	177.1 ± 8.9	175.8 ± 5.6
WEIGHT (kg)	77.7 ± 10.3	76.9 ± 11.4	78.4 ± 9.04

Values are means ± SD.

Table 2

BASELINE VENTILATORY VARIABLES

	ALL (n=47)	NONSMOKERS (n=22)	SMOKERS (n=25)
$\dot{V}_E$	12.9 ± 2.79	13.9 ± 2.9	12.0 ± 2.4*
$P_{et}CO_2$	37.7 ± 2.5	37.6 ± 2.6	37.8 ± 2.5
HVR	1.04 ± 0.74	1.00 ± 0.78	1.08 ± 0.70
(Range)	(0.01 to 4.04)	(0.22 to 4.04)	(0.01 to 3.44)
HCVR	2.12 ± 1.01	2.24 ± 1.06	2.02 ± 0.94
(Range)	(0.75 to 5.39)	(0.87 to 5.39)	(0.75 to 3.89)

Values are means ± SD except where noted.

*Significantly different from nonsmokers ($p < 0.05$)

$\dot{V}_E$ = Minute Ventilation, l/min; $P_{et}CO_2$ = End Tidal CO_2, Torr;

HVR = Hypoxic Ventilatory Response, $\Delta \dot{V}_E / \Delta SaO_2$ = Arterial Oxygen Saturation, %;

HCVR = Hypercapnic Ventilatory Response, $\Delta \dot{V}_E / \Delta P_{et}CO_2$.

Table 3

FACTOR SCORES DERIVED FROM THE ENVIRONMENTAL SYMPTOMS QUESTIONNAIRE

	ALL (n=47)	NONSMOKERS (n=22)	SMOKERS (n=25)
AMS-c	0.52 ± 0.40	0.51 ± 0.36	0.53 ± 0.42
(Range)	(0.00 to 1.63)	(0.00 to 1.17)	(0.00 to 1.63)
AMS-r	0.52 ± 0.36	0.45 ± 0.33	0.58 ± 0.36
(Range)	(0.00 to 1.50)	(0.00 to 0.94)	(0.04 to 1.50)

Values are means ± SD except where noted.

AMS-c and AMS-r are the "Cerebral" and "Respiratory" factor scores, respectively, of the Environmental Symptoms Questionnaire.

Table 4

NUMBER OF SUBJECTS DEVELOPING AMS

	ALL (n=47)	NONSMOKERS (n=22)	SMOKERS (n=25)
AMS-c (>0.7)	16 (34%)	8 (36%)	8 (32%)
AMS-r (>0.6)	14 (30%)	4 (18%)	10 (40%)
EXCEEDING ONE OR BOTH CRITERION SCORES	18 (38%)	8 (36%)	10 (40%)

AMS-c and AMS-r are the "Cerebral" and "Respiratory" factor scores, respectively, of the Environmental Symptoms Questionnaire.

Table 5

VENTILATORY VARIABLES OF THOSE WHO DID AND DID NOT DEVELOP AMS

(exceeding at least AMS-C > 0.70 or AMS-R > 0.60)

	NONSMOKERS (n=22)		SMOKERS (n=25)	
	Sick (n=8)	Not Sick (n=14)	Sick (n=10)	Not Sick (n=15)
$\dot{V}_E$	13.9 ± 2.91	13.9 ± 2.8	12.2 ± 2.41	12.0 ± 2.4
$P_{et}CO_2$	36.9 ± 1.67	38.0 ± 2.9	37.0 ± 2.41	38.4 ± 2.3
HVR	1.03 ± 0.31	0.99 ± 0.95	1.14 ± 0.89	1.03 ± 0.52
(Range)	(0.69 to 1.49)	(0.22 to 4.04)	(0.01 to 3.44)	(0.34 to 2.10)
HCVR	2.26 ± 0.91	2.22 ± 1.14	2.16 ± 0.94	1.93 ± 0.94
(Range)	(1.49 to 4.17)	(0.87 to 5.39)	(0.75 to 3.64)	(0.80 to 3.89)

Values are means ± SD except where noted.

$\dot{V}_E$ = Minute Ventilation, l/min; $P_{et}CO_2$ = End Tidal CO_2, Torr;

HVR = Hypoxic Ventilatory Response, $\Delta \dot{V}_E/\Delta SaO_2$ = Arterial Oxygen Saturation, %;

HCVR = Hypercapnic Ventilatory Response, $\Delta \dot{V}_E/\Delta P_{et}CO_2$.

Table 6

CORRELATION COEFFICIENTS BETWEEN THE VENTILATORY TESTS AND THE AMS FACTOR SCORES

	ALL (n=47)	NONSMOKERS (n=22)	SMOKERS (n=25)
HVR vs AMS-c	0.16	0.16	0.16
HCVR vs AMS-c	0.07	0.09	0.05
HVR + HCVR vs AMS-c	0.16	0.16	0.17
HVR vs AMS-r	0.02	0.05	0.09
HCVR vs AMS-r	0.04	0.04	0.08
HVR + HCVR vs AMS-r	0.04	0.05	0.10

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